UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LAURENT COEN, ROSARIO OSTA PINZOLAS, and PHILIPPE BRULET

Appeal No. 2005-1441
Application No. 09/816,467

HEARD: October 6, 2005

DECISION ON APPEAL

ELLIS, MILLS and GRIMES, Administrative Patent Judges.

ELLIS, Administrative Patent Judge.

This is appeal pursuant to 35 U.S.C. § 134 from the examiner's final rejection of claims 17, 18, 21-23, 34 and 35.

Claim 17 is representative of the subject matter on appeal and reads as follows:

17. A hybrid fragment of tetanus toxin comprising a fragment C and a fragment B or a fraction of fragment B having at least 11 amino acid residues, wherein the hybrid fragment is capable of transferring in vivo a protein, a peptide, or a polynucleotide through a neuromuscular junction and at least one synapse.

The references relied upon by the examiner are:

Gregory P. Mueller, Ph.D. (Mueller), "Toxin-Mediated Transfer and Expression of Genes in Nerve Cells" NTIS Accession No. ADA290501, ARO CONTRACT 118-92, ARO#-27890 -LS, pp.1-15 (October 12, 1994).

Barbara Höhne-Zell et al., (Höhne-Zell), "Functional Characterization of the Catalytic Site of the Tetanus Toxin Light Chain Using Permeabilized Adrenal Chromaffin Cells" FEBS Letters, vol. 336, No. 1, pp 175-180 (December 1993).

All the claims stand rejected under 35 U.S.C. § 103 as being unpatentable in view of Mueller and Höhne-Zell.

We have considered the respective positions of both the examiner and the appellants and find ourselves in substantial agreement with that of the appellants. Accordingly, we reverse.

Background

The specification discloses that:

> Tetanus toxin is a potent neurotoxin of 1315 amino acids that is produced by Clostridium tetani .... It prevents the inhibitory neurotransmitter release from spinal cord interneurons by a specific mechanism ... [which] has been demonstrated to involve retrograde axonal and transynaptic transport of the tetanus toxin [specification, p. 8].
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> Tetanus toxin is produced ... as an inactive, single, polypeptide chain of 150 kD composed of three 50 kD domains connected by protease-sensitive loops. The toxin is activated upon selective proteolytic cleavage, which generates two disulfide-linked chains: L (light, 50 kD) and H (heavy, 100 kD).... [id., p. 1].

The specification further discloses that the enzyme papain is able to "cleave[] the tetanus toxin into two fragments: - the C terminal part of the heavy chain, 451 amino acids also called fragment C; and - the other part contained the complementary portion called fragment B linked to the light chain (fragment A) via a disulfide bond." Specification, p. 2. Prior to the appellants' invention it was known in the art that fragment A has a zinc-binding domain which is responsible for the toxic properties of the protein. Höhne-Zell, p. 175, the abstract and col. 2; Mueller, p. 3, last para. It was also known that fragment C of the toxin molecule is responsible for binding "to high affinity receptors located on presynaptic terminals outside the blood-brain barrier" which results in internalization of the toxin. Mueller, p. 3, last para. "Once internalized the toxin is transported retrogradely to neuronal cell bodies, its presumed site of toxic action." Id.

As indicated by claim 17 above, the present invention is directed to a composition which comprises only fragment C and at least 11 amino acids of fragment B. Said composition is said to be useful for transporting proteins, peptides and polynucleotides through a neuromuscular junction and at least one synapse.

Discussion

The examiner has based his conclusion of obviousness on the combined teachings of Mueller and Höhne-Zell. In this regard, the examiner points to the teachings of Mueller (I) of "receptor mediated gene transfer in the central nervous system"; (ii) "'tetanus toxin is uniquely specific for uptake into neurons and enters the central nervous system from the circulation with the highest efficiency of any known protein'"; (iii) "that the carboxy terminal

(C-fragment) of the protein [tetanus toxin] alone is not toxic and is sufficient for internalization and transport (retrograde) as a carrier molecule for neuron specific gene transfer in vivo"; (iv) "the toxic portion of the protein resides in the amino terminal." Answer, p. 4.

The examiner acknowledges that Mueller does not disclose a hybrid fragment containing either fragment B or a portion of fragment A which is devoid of its toxin activity, but argues that the teachings of Höhne-Zell make up for this deficiency. Id.

In this regard, the examiner points out that Höhne-Zell discloses that "the replacement of histidine (position 233) by cysteine or valine and of glutamate (position 234) b

y glutamine completely abolished the activity of" fragment A.

The examiner concludes that

> It would have been obvious for one of ordinary skill at the time of the invention to generate [the] claimed hybrid fragment or composition because Mueller teaches that the C-fragment of the tetanus toxin alone is not toxic and the toxic portion of the protein resides in the amino terminal and in combination with the teaching of Höhne-Zell that the putative zinc-binding domain constitutes the active site of the tetanus toxin light chain would make it obvious . . . to remove said zinc-binding domain when generating a tetanus toxin fragment for neuron specific transport. It also would have been obvious for one of ordinary skill at the time of the invention to include a portion of fragment B with fragment C of the tetanus toxin because the toxic region of tetanus toxin resides in the putative zinc-binding domain, which is at [the] amino terminal, and inclusion of a portion of non-toxic region of tetanus toxin would not contribute to the toxicity of tetanus toxin [Answer, pp. 4-5].

We find the examiner's position untenable.

It is well established that the examiner has the initial burden under § 103 to establish a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Piasecki, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). To that end, it is the examiner's responsibility to show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art, would have led one of ordinary skill in the art to combine the references to arrive at the claimed invention. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

Here, we find that the examiner has not provided any reason based on the applied prior art as to why the claimed invention would have been obvious to one of ordinary skill in the art. That is, if we look at the subject matter recited in claim 17, we find that it is directed to a composition which comprises, inter alia, a fragment C and at least 11 amino acids of fragment B of tetanus toxin. We agree with the examiner that Mueller teaches a composition which comprises fragment C [of tetanus toxin]; however, we do not find that Mueller teaches or suggests that the composition further comprise fragment B, or an 11 amino acid portion thereof. To the contrary, Mueller appears to suggest that fragment C alone is "sufficient for internalization and transport, and therefore could be . . . utilized as a carrier molecule for neuron specific gene transfer in vivo." Mueller, p. 4. Nor do we find that Höhne-Zell teach or suggest the use of the tetanus toxin fragment B in any regard. Rather, on this record, the only place where we find any suggestion to construct a hybrid fragment of tetanus toxin having each of the elements recited in the claims is in the

appellants' specification. Thus, we find that the examiner has engaged in impermissible hindsight to arrive at his conclusion that the claimed invention would have been obvious over Mueller and Höhne-Zell. In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991)("It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps"); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985); W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984)("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest

that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher").

Accordingly, the rejection is reversed.

REVERSED

JOAN ELLIS
Administrative Patent Judge

DEMETRA J. MILLS
Administrative Patent Judge

ERIC GRIMES
Administrative Patent Judge

) BOARD OF PATENT APPEALS AND INTERFERENCES

JE/lp

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER
LLP
1300 I STREET, NW
WASHINGTON, DC 20005